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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Syken et al.	Group Art Unit: 1632
Serial No.: 09/908,992	Examiner: Li, Q.
Filing Date: July 19, 2001	Attorney Docket No.: H MV-054.01
For: <i>Methods and Reagents to Regulate Apoptosis</i>	

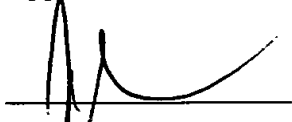
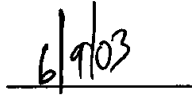
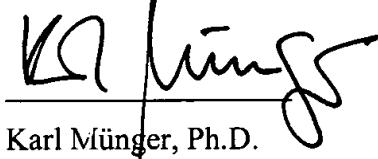
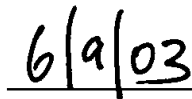
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Declaration of J. Syken and K. Münger/under 37 C.F.R. § 1.132

Sir:

1. We, Joshua Syken, a citizen of the United States, residing at 19 Goldsmith Street, Jamaica Plain, Massachusetts and Karl Münger, a citizen of the Switzerland, residing at 33 Goddard Street, Newton, Massachusetts, hereby declare as follows:
2. I, Joshua Syken, Ph.D., am a Postdoctoral fellow, Department of Neurobiology, Harvard Medical School, Boston, Massachusetts. A copy of my curriculum vitae and list of publications are attached hereto as Exhibit A.
3. I, Karl Münger, Ph.D., am an Associate Professor, Department of Pathology, Harvard Medical School, Boston, Massachusetts. A copy of my resume and list of publications are attached hereto as Exhibit B.
4. We are co-inventors in the above-referenced patent application.
5. We understand that the publication Syken et al. (Proc. Natl. Acad. Sci. U.S.A. 96:8499-8504 (1999)) was cited against the above-referenced patent application.
6. We are the sole inventors of the experimental work described in Syken et al, *supra*.
7. Dr. Tali De-Medina, Ph.D., coauthor of Syken et al., *supra*, is not a co-inventor in the above-referenced application. Dr. De-Medina performed experiments confirming our initial observation that Tid1S localized to the mitochondria. Accordingly, Dr. De-Medina did not contribute to our invention as set forth in this patent application.
8. We declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further, that these

statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.


Joshua Syken, Ph.D.
Date
Karl Munger, Ph.D.
Date

Josh Syken, Ph.D.
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Education/Research Experience

1992-1995

B.S., Purchase College, Purchase NY
Advisor: Dr. Elysse Craddock

1995-1999

Ph.D., Harvard Medical School
Advisor: Dr. Karl Munger
Thesis: TID1 Encodes Two Mitochondrial Modulators of Apoptosis with Opposing Functions

2000-Present

Postdoctoral fellow
Harvard Medical School
Advisor: Dr. Carla Shatz

Awards and Honors

1992 - CRC Chemistry Award, Purchase College
1992-1995 - William D. Schlutow Scholarship for Excellence in Biology,
Purchase College.
1995 - Purchase College Presidents Achievement Award
1995 - Summa Cum Laude, Purchase College
1997-1999 - Ryan Fellow, Harvard Medical School
2000-Present - NIH NRSA Postdoctoral Fellowship

Publications

Schilling B, De-Medina T, Syken J, Vidal M, Munger K. 1998. A novel human DnaJ protein, hTid-1, a homolog of the Drosophila tumor suppressor protein Tid56, can interact with the human papillomavirus type 16 E7 oncoprotein. Virology. 1998 247(1):74-85

Syken J, De-Medina T, Munger K., 1999
TID1, a human homolog of the Drosophila tumor suppressor l(2)tid, encodes two mitochondrial modulators of apoptosis with opposing functions. Proc Natl Acad Sci U S A. 96(15):8499-504

Syken, J., Macian, F., Agarwal, S., Rao, A., Munger, K., 2003. TID1, a Mammalian Homolog of the Drosophila Tumor Suppressor lethal(2) tumorous imaginal discs Regulates Activation-Induced Cell Death in Th2 Cells. Oncogene, In Press.

CURRICULUM VITAE

PART I: General Information

DATE PREPARED: June 5, 2003

Name: Karl M \ddot{u} nger

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Place of Birth: Z \ddot{u} rich, Switzerland

Education:

1981 B.Sc. (Biochemistry), University of Z \ddot{u} rich, Switzerland

1986 Ph. D. (Biochemistry), University of Z \ddot{u} rich, Switzerland

Postdoctoral Training:

1986-1990 Viral Oncology, Laboratory of Tumor Virus Biology, National Cancer Institute, NIH, Bethesda, MD

Professional Appointments:

1990-1993 Visiting Associate, Laboratory of Tumor Virus Biology, National Cancer Institute, NIH, Bethesda, MD

1993-present Member, Board of Tutors in Biochemical Sciences, Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA.

1993 –1998 Assistant Professor, Department of Pathology, Harvard Medical School, Boston, MA

1998-present Associate Professor, Department of Pathology, Harvard Medical School, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1995	Consultant, WHO/IARC Working Group on Human Papillomaviruses
1995-1996	Faculty Member, Histopathobiology of Neoplasia Workshop, organized by the American Association for Cancer Research
1996	Visiting Professor, Department of Biology, University of Padua, Italy
1999	Consultant, Boston BioProducts, Inc., Ashland, MA
1999	Consultant, McKinsey and Company
2001-date	Consultant, National Toxicology Program, Evaluation of HPV as a Carcinogen
2002	Consultant, Pharmacia-Upjohn Company, Kalamazoo, MI.
2002	Faculty Member, Pathobiology of Cancer Workshop, organized by the American Association for Cancer Research
2002-present	Consultant, Arbor Vita Corporation, Sunnyvale CA

Major Committee Assignments:

1996	Temporary Member, Experimental Virology Study Section, National Institutes of Health
1996	Scientific Committee, 15th International Papillomavirus Workshop, Queensland, Australia 1996
1997	Temporary Member, Experimental Virology Study Section, National Institutes of Health
1998	Chairman, Viral Oncology Section, Program Committee, American Association for Cancer Research, Annual Meeting.
1998	Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.
1998	Member, NIH Special Emphasis Panel (ZRG5 EVR-01) Study Section
1998	Member, NIH Site Visit Committee for Program Project 1 P01 DE2704-01.
1998	Member, NIH Site Visit Committee for Program Project 1 P50 DC00203-15A1
1998-2001	Cancer Research Campaign (UK), Outside Reviewer
1999	Scientific Program Committee, 17th International Papillomavirus Workshop, Charleston, SC.
1999	Grant Reviewer, National Science Foundation of Austria
1998	Member, NIH Special Emphasis Panel (DE 98-008)
1999	Temporary Member, NIDCR Special Emphasis Panel
2000-2001	Review Board, NIGM/NIH Intramural Postdoctoral Fellowship Program (PRAT Fellowships)

2000, 2003 Grant Reviewer, Dutch Cancer Society.
2000 Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.
2000-date Member NIDCR Special Review Panel.
2000-date Tenure Reviewer for Tufts University (2), Case Western University, Cleveland OH, University of Massachusetts, The Hebrew University of Jerusalem (Israel)
2000-2004 Regular Member, NIH Study Section “Virology”.
2001, 2003 Grant Reviewer, National Science Foundation, Austria.
2001 Grant Reviewer, Italian Association for Cancer Research
2001 Scientific Program Committee, 19th International Papillomavirus Workshop, Florianopolis, Brazil
2002 Grant Reviewer, Ohio Cancer Research Associates.
2002 Grant Reviewer, Sass Fellowship Foundation
2002, 2003 Grant Reviewer, Department of Veterans Affairs
2002 Member, NIDCD Special Review Panel 020628.
2002 Organizing Committee, International Conference on Small DNA Tumorviruses, Madison, WI.
2002 Grant Reviewer, Research Management Group, Linthicum Heights, MD
2002 Grant Reviewer, Cancer Research UK
2003 Nomination Committee, NIGM/NIH Intramural Postdoctoral Fellowship Program (PRAT Fellowships)
2003 Member, Viral Oncogenesis and Mechanisms Section of the Cellular, Molecular, and Tumor Biology Subcommittee of the Program Committee for the Annual Meeting of the American Association for Cancer Research.
2003 Member, NIH Site Visit Committee for Program Project 1 P01 CA16038-31
2004 Scientific Committee, 21st International Papillomavirus Conference

Professional Societies:

Swiss Society for Biochemistry
American Society for Microbiology
American Association for Cancer Research
American Society for Investigative Pathology
Boston Cancer Research Association (Massachusetts Section of the American Association for Cancer Research), Vice President 1997-1998; President 1998-1999
International Papillomavirus Society

Community Service Related to Professional Work:

- 2001 Mentor, Outside Researchers Session, Excellence Through Diversity Initiative,
Doctoral Scholars Program, New England Board of Higher Education.
- 2003 Mentor, Minorities in Cancer Research Council of the AACR, Symposium:
“Navigating the Road to a Successful Career in Cancer Research”

Editorial Boards:

- 1995-present Journal of Virology
- 1998-present Virology
- 2001-present Cancer Research; Associate Editor
- 2001-present Cancer Biology & Therapy; Associate Editor
- 2003-present Molecular Cancer

Ad hoc reviewer for: Am. J. Pathol., Biochemistry, Biochem. Biophys. Acta, Br. J. Cancer.,
Cancer, Cancer Detection and Prevention, Cancer Invest., Cell, Cell Death
Diff., Cell Growth Diff., Clin. Canc. Res., EMBO J., Exp. Cell Res., Gene,
Genes & Development, Genes, Chromosomes and Cancer, Gynecol.
Oncol., Int. J. Cancer, IUBMB Life, J. Cell Science., J. Clin. Invest., J.
Clin. Oncol., J. Exp. Med, J. Immunol., J. Natl. Canc. Inst., Mol. Cell
Biol., Mol. Pharmacol., Microbiol. Mol. Biol. Reviews., Nature, Nature
Cell Biology, Nature Medicine, Nucl. Acids Res., Oncogene, Oncol. Res.,
Proc. Natl. Acad. Sci. USA, Science, Trends in Microbiology, Virus Res.

Awards and Honors:

- 1986-1988 John E. Fogarty Postdoctoral Fellowship
- 1989 Advanced Training Fellowship, Swiss National Science Foundation
- 1990 Dr. Ernst Th. Jucker Award for Experimental Cancer Research, Zurich,
Switzerland
- 1996-1998 Junior Faculty Research Award, American Cancer Society
- 1998-2000 Ludwig Scholar

Funding

Past:

- 1/94-12/94 Funds for Discovery; PI; “Disruption of dimer formation as a strategy to
inactivate the HPV E7 oncoprotein.”
- 1/94-12/94 Milton Fund; PI; “Protein domains governing the transformation function of the
HPV E7 oncoprotein.”
- 1/94-12/98 American Cancer Society; PI; “Characterization of cellular factors associated with
the HPV E7 protein” (#VM97; #RPG-94-011-04-VM).

- 1/95-12/97 Council for Tobacco Research; PI; “Viral oncoproteins as probes to study cellular growth regulation” (#3859).
- 1/96-12/98 American Cancer Society; PI; “The role of HPV E7 in cervical carcinogenesis” (JFRA-597)
- 6/97-5/98 National Institutes of Health; PI; “The role of basic helix-loop-helix (bHLH) proteins in epithelial cell proliferation and differentiation”; Pilot and Feasibility Project Grant; P30 AR42689 (T.S. Kupper, PI).
- 4/99-3/00 GLAXO-WELLCOME Co., PI; “Alteration of Cellular Signal Transduction Pathways by the Human Papillomavirus E7 Oncoprotein”; Industry-sponsored Research Grant.
- 7/99-6/01 Hoechst Marion Roussel Co., “Modulation of TID1 During T-Cell Activation: Implications for Activation Induced Cell Death” Industry sponsored Research Grant.
- 4/98-3/03 Project leader; National Institutes of Health; “Cell cycle dysregulation in oral cancer”; Program Project Grant P01 DE012467 (David T. Wong, PI).

Current:

- 4/96-6/05 Principal Investigator: National Cancer Institute/National Institutes of Health; “Biological activity of HPV E7 in human epithelial cells” (R01 CA66980).
- 9/02-6/05 Principal Investigator: National Cancer Institute/National Institutes of Health; “Biological activity of HPV E7 in human epithelial cells”- Competitive Supplement (3R01CA066980-7S1)
- 2/00-1/05 Principal Investigator: National Cancer Institute/National Institutes of Health; “Modulation of Host Cell Apoptotic Responses by HPV E7” (R01 CA81135).
- 10/01-9/06 Project Co-investigator; National Heart, Lung, and Blood Institute/National Institutes of Health; “Adhesion molecules in transfusion biology” Program Project Grant 2P01 HL56949 (Denisa Wagner, P.I.).
- 7/02-6/03 Co-investigator: Stewart Trust; “Identification of cellular markers of human cervical preneoplasia by Serial Analysis of Gene Expression (SAGE)”
- 12/02-11/04 Principal Investigator: Astra-Zeneca; “Tripeptidyl transferase II and c-myc induced centrosome mediated genomic instability”
- 6/03-5/05 Co-Principal Investigator: CYTYC Corporation; “Cellular markers of cervical neoplasia
- 7/03-11/07 Project Co-investigator: National Cancer Institute/National Institutes of Health; “Spectroscopic imaging and diagnosis of neoplasia” Bioengineering Research Partnership CA097966-01; (Michael Feld, MIT, P.I.)

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Original Articles:

1. M \ddot{u} nger K, Lerch K, Tschierpe HJ. Metal accumulation in *Agaricus bisporus*: influence of Cd and Cu on growth and tyrosinase Activity. *Experientia* 38:1039-1041, 1982.
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3. M \ddot{u} nger K, Germann UA, Lerch K. Isolation and structural organization of the *Neurospora crassa* copper metallothionein gene. *EMBO J.* 4:2665-2668, 1985.
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5. M \ddot{u} nger K, Germann UA, Lerch K: The *Neurospora crassa* copper metallothionein gene: regulation of expression and chromosomal location. *J. Biol. Chem.* 262:7363-7367, 1987.
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7. M \ddot{u} nger K, Lerch K. Peptide mapping of vertebrate and invertebrate metallothioneins. *Inorganica Chimica Acta* 151:11-13, 1988.
8. Phelps WC, Yee CL, M \ddot{u} nger K, Howley PM. The human papillomavirus type 16 E7 gene encodes transactivation and transformation functions similar to adenovirus E1a. *Cell* 53:339-347, 1988.
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10. Dyson N, Howley PM, M \ddot{u} nger K, Harlow, E. The human papillomavirus type 16 E7 oncoprotein is able to bind the retinoblastoma gene product. *Science* 243:934-937, 1989.
11. M \ddot{u} nger K, Phelps WC, Bubb V, Howley PM, Schlegel R. The E6 and E7 genes of the human papillomavirus type 16 together are necessary and sufficient for transformation of primary human keratinocytes. *J. Virol.* 63:4417-4421, 1989.
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35. Jones DL, Thompson, DA, Munger K. Destabilization of the pRB tumor suppressor protein and stabilization of p53 contribute to HPV type 16-induced apoptosis. *Virology* 239:97-107, 1997.
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38. Timmermann S, Hinds PH, Munger K. Reexpression of endogenous p16ink4a in oral squamous cell carcinoma lines by 5-aza-2'-deoxycytidine induces a senescence-like state. *Oncogene* 17:3445-3453, 1998.
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40. Syken J, De-Medina T, Munger K. hTid-1, the human homolog of the Drosophila tumor suppressor Tid56, is a mitochondrial regulator of apoptosis. *Proc. Natl. Acad. Sci. USA* 96:8499-8506, 1999.
41. Alani RM, Hasskarl J, Grace M, Hernandez MC, Israel MA, Munger K. immortalization of primary human keratinocytes by the helix-loop-helix protein, Id1. *Proc. Natl. Acad. Sci. USA* 96:9637-9641, 1999.
42. Oettgen P, Kas K, Dube A, Gu X, Grall F, Thamrongsak U, Akbarali Y, Finger E, Boltax J, Endress G, Munger K, Kunsch C, Libermann TA. Characterization of ESE-2, a novel

- ESE-1-related ets transcription factor that is restricted to glandular epithelium and differentiated keratinocytes. *J. Biol. Chem.* 274:29439-29452, 1999.
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60. Riley R, Duensing S, Brake T, Munger K, Lambert PF, Arbeit JM: Dissection of human papillomavirus E6 and E7 function in transgenic mouse models of cervical carcinogenesis, submitted
61. Basile JR, Zacny V, Eichten A, Munger K: TRAIL/APO2L signaling in primary human keratinocytes does not involve rapid anti-apoptotic NF- κ B activation, submitted
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